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EXAMINER

KELLY, ROBERT M

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/971,773

Applicant(s)

KANDA ET AL.

Examiner

Robert M Kelly

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34,36-61 and 63-68 is/are pending in the application.
- 4a) Of the above claim(s) 5-11,21,22,24-30 and 41-61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,12-20,23,31-40 and 63-68 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 August 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 8/12/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and arguments of 12 August 2004 have been entered.

Claims 35 and 62 have been cancelled.

Claims 1-2, 4, 12, 16-19, 23, and 63 are amended.

Claims 65-68 are newly added.

Election/Restrictions

Applicant now traverses the restriction requirement of 10 June 2003, arguing that Group I should be rejoined with Group II because the subject matter necessarily requires a review of the same art, and the fact that the Examiner considered the common claim to both groups: Claim 1 (Applicant's Response of 12 August 2004, pp. 29-30).

It is noted that Applicant did not traverse the restriction requirement in the response to restriction, received by this office on 8 December 2003, pp. 24-25. As such, the Response to Restriction Requirement of 8 December 2003 was treated as an election without traverse (Official Action of 13 February 2004, p. 2). However, the Examiner recognizes that Applicant has made a persuasive argument, and that, indeed, the Examiner did examine some aspects of Group I. Claim 2 was substantively considered in Claim 19, Claim 3 was substantively considered in Claim 64, and Claim 20 was substantively considered in Claim 39. (Further evidence that Applicant was aware of the substantive consideration of these claims is evidenced by Applicant's amendments, which amends Claim 2 in a manner consistent with Claim 19. (Applicant's Response of 12 August 2004, pp. 3 and 9).) Moreover, it is recognized that Applicant has amended Claims 2-3 and 20 to read within the scope of the presently considered invention. Therefore, Claims 2-3 and 20 will be rejoined with the consideration of Group II;

Art Unit: 1632

however, since the Applicant did not traverse this requirement until after a First Action on the Merits, and because these aspects were already rejected in the First Action on the Merits, new rejections to these claims are not considered to preclude finality, unless such rejections were not applied to the previously examined claims in the prior Office Action.

Therefore, Claims 1-20 and 23-40 are now all within the scope of the invention of Group II, and Claims 5-11 and 24-30 remain withdrawn from prosecution until such time as a generic claim is found otherwise allowable with respect to the elected species.

The restriction requirement is made FINAL.

Hence, Claims 1-4, 12-20, 23, 31-40, and 63-68 are presently considered with respect to the elected species.

This application contains claims 21-22 and 41-61 drawn to an invention nonelected with traverse in Applicant's responses of 17 September 2003 and 12 August 2004. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of

Art Unit: 1632

nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression “now Patent No. _____” should follow the filing date of the parent application. If a parent application has become abandoned, the expression “now abandoned” should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was

due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

While the PCT document may be obtained, a certified copy of the Japanese language Applications, translated into English, is required.

Priority – Response to Arguments

Applicant has amended the first paragraph of the specification to properly recite priority to Applicant's priority documents. Moreover, Applicant has stated that "Certified copies and English translations of the priority documents will be forwarded under separate cover." (Applicant's response of 12 August 2004, p. 28, first paragraph). However, no such certified copies have been received at this time.

Therefore, the objection to Applicant's priority for lacking English translations, while currently held, will also be held in abeyance until such time as the English translations are made available to the Examiner or Applicant's claims are found otherwise allowable.

Information Disclosure Statement

The information disclosure statement filed 12 August 2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. It is noted that WIPO documents 97/27303A1 and 00/61739A1 are written in a

Art Unit: 1632

foreign language, but provide an English language abstract, and therefore, these abstracts have been considered, as noted on the IDS. It is further noted that the reference to Furukawa, et al. (1998) Nucleic Acid and Enzyme, 43: 2309-17 was not provided with such English-language translation; hence a line has been drawn through such reference on the IDS. The examiner has not considered the reference of Furukawa, et al.

Specification

In light of Applicant's amendments and arguments of 12 August 2004, the objection to the specification is withdrawn.

Claim Objections – Old

In light of Applicant's amendments and arguments of 12 August 2004, the objection to Claim 1 is withdrawn.

Claim Objections – New – Necessitated by Amendment

Claims 2, 19, and 63 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 2, 19, and 63 require that fucose is not linked to a reducing-end N-Acetylglucosamine through alpha-1,6 linkages in complex sugar chains; however, they depend from Claims 1, 18, and 4, respectively, referring to complex sugar chains in which fucose is not linked to a penultimate N-Acetylglucosamine at all. Therefore, Claims 2, 19, and 63 do not further limit Claim 1, 18, and 4, respectively. Such rejection is made now because it was unclear what the Applicant was claiming during the first action on the merits, as reflected in the rejection under 35 USC 112, second paragraph rejection in the Official Action

Art Unit: 1632

of 13 February 2004, p. 6. Moreover, as noted in rejoinder of Claim 2 (Above, pp. 2-3) Claim 2 has been rejoined as of this action, but rejections and objections to this Claim do not remove the necessity of making this action final.

Claim Rejections - 35 USC § 112, second paragraph – Old rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In light of Applicant's amendments and arguments of 12 August 2004, the rejection of Claims 4, 12-19, 23, 31-40, and 63 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn.

In light of Applicant's cancellation of Claim 62, the rejection of Claim 62 under 35 USC 112, second paragraph, as being indefinite, is moot, and therefore, withdrawn.

Claim Rejections - 35 USC § 112, second paragraph, Necessitated by Amendment

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1, 12, 19, and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 limits the enzyme relating the modification of complex N-glycoside-linked sugar chains in which fucose is bound to the 6-position of the N-acetylglucosamine in the

Art Unit: 1632

reducing end to the enzyme alpha-1,6-fucosyltransferase. It is not clear how this enzyme, which places such fucose onto N-acetylglucosamine is related to the modification of chains already containing such fucose linked to N-acetylglucosamine.

Claims 2, 19, and 63 limit Claims 1, 18, and 62, respectively, to reducing-end N-Acetylglucosamines substituted with fucose at the 6 position of N-Acetylglucosamine. It is unclear how fucose could be bound through the 6 position in Claims 2, 19, and 63, if it is already not bound in parent claims 1, 18, and 62.

Claim Rejections - 35 USC § 112 – New Matter, Necessitated by Amendment

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 4 and 23 encompass enzymes relating to the modification of a complex N-glycoside-linked sugar chain in which fucose is bound to the 6-position of N-Acetylglucosamine. While the specification does discuss alpha-1,6-N-Fucosyltransferase, no enzymes are disclosed for the modification of such bound sugars once they are bound. While Applicant directs the attention of the Examiner to Example 14 for support (Applicant's response of 12 August 2004, p. 31, first paragraph), such Example discusses the same alpha-1,6-N-Fucosyltransferase and not

Art Unit: 1632

any enzyme relating to the modification of existing fucose bound to N-Acetylglucosamine in such complex sugars.

This is a new matter rejection.

Claim Rejections - 35 USC § 112 – Enablement, old rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 12-19, 23, 31-40 and 62-64 remain rejected, and Claims 2-3, 20, and 65-68 are newly rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a CHO cell comprising a deletion of at least exon 2 of one FUT8 gene, which deletion produces a non-functional enzyme, into which a gene encoding an antibody is introduced, such antibody gene being expressed and producing antibodies having complex N-glycoside-linked sugar chains bound to the Fc region, wherein among the total complex N-glycoside-linked sugar chains bound to the Fc region in the composition, the ratio of a sugar chain in which fucose is not bound to N-acetylglucosamine at the 6 position is 20% or more, does not reasonably provide enablement for any CHO cell or any CHO cell comprising any deletion of a gene encoding FUT8 that produces any decrease in such enzyme, into which a gene encoding an antibody is introduced, such antibody gene being expressed and producing antibodies having complex N-glycoside-linked sugar chains bound to the Fc region, wherein among the total complex N-glycoside-linked sugar chains bound to the Fc region in the composition, the ratio of a sugar chain in which fucose is not bound to N-acetylglucosamine is

20% or more. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

It is noted that newly rejected Claims 2-3, 20, and 65-68, while encompassing limitations in glycosylation characteristics, antibody characteristics, methods of making antibodies, methods of making the CHO cells, do not encompass limitations which are considered lacking in this rejection.

Response - 35 USC § 112 – Enablement, old rejection

Applicant argues that the Specification enables teaches much more than the exemplified embodiments; that the Artisan would be able to make the mutants with the decreased or deleted activity; and reviews examples of mutants that could be made to meet the requirements of the claims. Therefore, Applicant argues, the rejections of the claims under 35 USC 112, first paragraph, as lacking an enabling disclosure, should be withdrawn (Applicant's response of 12 August 2004, pp. 32-35).

Applicants arguments have been fully considered but are not persuasive. Applicant appears to be arguing that these mutants could be made, by way of examples of mutants that delete the activity of the enzyme being mutated (Id., all examples). Applicant's papers discuss the divergent evolution of fucosyltransferases (Oriol, et al. (1999) Glycobiology, 9: 323-334); conserved structural features of such fucosyltransferases (Breton, et al. (1998) Glycobiology, 8(1) 87-94); knockout mice of a specific fucosyltransferase (Asano, et al. (1997) EMBO J., 16(8): 1850-57); and fucosyltransferase roles in selectin ligand biosynthesis (Maly, et al. (1996) Cell, 86: 643-53). Through these, Applicant argues that specific areas of the protein are

considered important, and therefore the Artisan would know how to mutate the fucosyltransferase in a reasonably predictable manner in order to knock-out the activity of the enzyme and thus prepare the cell (Applicant's arguments of 12 August 2004, p. 35, paragraph 1). However, Applicant's claims specifically embrace mutants that have decreased activity (e.g., Claims 4 and 23). It is maintained that Applicant still has not provided an enabling disclosure based on even one single enzyme mutation that decreases the activity of such enzyme to the proper amount, in CHO cells and thereby allows such cells to produce the claimed characteristic glycosylations (e.g., Official Action of 13 February 2004, p. 7, first paragraph, "... that produces any decrease in such enzyme [activity] ..."). Applicant has only demonstrated the ability to completely remove activity in a reasonably predictable manner (Id.).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of Applicant's amendments and arguments of 12 August 2004, the rejection of Claim 1 under 35 U.S.C. 102(b) as being anticipated by Lifely, et al. (1995) *Glycobiology*, 5(8): 813-22, is withdrawn.

CONCLUSION

The claims are free of the art of record.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M Kelly whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1632

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Anne M. Wehbe', with a long horizontal stroke extending to the right.